As the examiner is aware, patents preferably *omit* what is well known in the art. Manual of Patent Examining Procedure, § 2164.01 (8th ed., August 2001). Consequently, "the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent *coupled with information known in the art* without undue experimentation." *Id.* (quoting *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988)) (emphasis added). Furthermore, experimentation is not "undue" simply because it may be complex, expensive, or time-consuming. *Id.*, §§ 2164.01 and 2164.06 (citing, for example, *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983); *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); *In re Colianni*, 561 F.2d 220, 224 (CCPA 1977);*United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988)).

A variety of pharmaceutically acceptable prodrugs are well known to those of ordinary skill in the art. These include, but are not limited to, biohydrolyzable amides, esters, carbamates, carbonates, ureides, and phosphates. *See, e.g.*, U.S. Patent No. 5,654,302 at col. 2, lines 7-22 ("So-called prodrug esters, which in general enhance oral absorption and are hydrolyzed in vivo to form the active component of the ester, *have become quite common in the medicinal art*") (citing Bundgaard, H. *et al.*, *J. Med. Chem.*, 32:2503-7 (1989)) (emphasis added); U.S. Patent No. 5,760,021 at col. 9, lines 39-54 (providing examples of biohydrolyzable esters). Significantly, methods of making such prodrugs are also well known. *See, e.g.*, 1 Burger's Medicinal Chemistry and Drug Discovery, 172-178, 949-982 (5th ed., 1995); Design of Prodrugs, (H. Bundgaard ed., Elselvier, New York 1985). Therefore, based on the application as filed and information known in the art, a chemist of ordinary skill would be able to prepare pharmaceutically acceptable prodrugs of the compounds recited by the claims without undue experimentation. For this reason, Applicants respectfully request that the rejection of the claims under the first paragraph of § 112 be withdrawn.

B. The Provisional Double Patenting Rejection

On pages 2-3 of the Office Action, claims 1-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-5, 7-18, 20-24 and 36-39 of co-pending U.S. Patent Application No. 09/853,617. This is a provisional rejection. Consequently, if the Examiner maintains this rejection when the claims are otherwise deemed allowable, Applicants will take the necessary steps to overcome it (*e.g.*, by filing a Terminal Disclaimer).

Conclusion

As discussed above, this application is in condition for allowance, early notice of which would be appreciated.

No fee is believed to be due for the submission of this response. However, if any fees be required in order to enter this response into the file of the application and/or to avoid abandonment of the application, please charge such fees to Pennie & Edmonds LLP's Deposit Account No. 16-1150.

Respectfully submitted,

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